UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

IN RE: ZOFRAN (ONDANSETRON) PRODUCTS LIABILITY LITIGATION	**)**	**MDL No. 1:15-md-2657-FDS**
	)	This document relates to:
	)	All Actions

PLAINTIFFS' MEMORANDUM RELATED TO GSK'S MOTION FOR SUMMARY JUDGMENT BASED ON FEDERAL PREEMPTION IN LIGHT OF MERCK SHARP & DOHME CORP. V. ALBRECHT

In its February 5, 2019 Memorandum and Order, Doc. 1325, this Court denied GSK's motion for summary judgment based on federal preemption. The Court ruled that there was "at a minimum" a genuine disputed issue of material fact as to whether the FDA would have approved a birth defect warning for Zofran if it had been provided with material scientific information that GSK had withheld from the agency, such as the Japanese animal studies; therefore, the Court could not conclude that there was "'clear evidence' that the FDA would have rejected Plaintiffs' proposed label changes even if a more comprehensive disclosure had been made." Doc. 1325 at 44; *see also id.* at 51. Under the existing legal framework, prior to the Supreme Court decision in *Merck Sharp & Dohme Corp. v. Albrecht*, this Court concluded that summary judgment was improper because that question was a factual issue that must be resolved by a jury. Doc. 1325 at 4, 31–34.

On May 20, 2019, the Supreme Court issued its decision in *Merck Sharp & Dohme Corp. v. Albrecht*, 2019 WL 2166393 (May 20, 2019), and, later that same day, this Court directed the parties to address the issue of how this Court should proceed in light of the Supreme Court's decision. Doc. 1505. Although the *Merck* decision concludes that the preemption question, even where it raises factual issues, is to be decided by a court, not a jury, that conclusion should not alter this Court's ruling on GSK's summary judgment motion for one simple reason: in *Merck*, the

Supreme Court reiterated that only an actual, irreconcilable conflict between state and federal law will give rise to preemption; a hypothetical or potential conflict is insufficient. 2019 WL 2166393, at *8. Here there is no clear irreconcilable conflict between state and federal law because the FDA has never rejected a birth defect warning for Zofran after being presented with all relevant scientific information. Any purported conflict remains entirely hypothetical.

Thus, there is no reason for this Court to revisit its summary judgment ruling, either through a bench trial or a renewed summary judgment motion.

DISCUSSION

This Court's Summary Judgment Ruling

In its February ruling, this Court carefully and methodically reviewed the case law concerning "clear evidence" preemption and then applied the teachings of that case law to the facts in the present case. The Court summarized the issues thusly:

> to prevail, GSK must show (a) that it could not have changed the label, by the CBE process or otherwise, or (b) if it could, that there is clear evidence that the FDA would have rejected the label that plaintiffs contend state law would have required. . . .
>
> Plaintiffs do not dispute that the FDA rejected enhanced warning labels on multiple occasions, and that those rejected labels in substance contain the same warnings plaintiffs say GSK should have provided. They contend, however, that GSK could have unilaterally changed its label through the CBE process after the initial label had been approved. They further contend that the FDA's rejection of proposed changes to the label, through the citizen petition and the Novartis application, were based on incomplete evidence, because GSK withheld information from the agency. According to plaintiffs, had the FDA been presented with that information, it would have required substantially stronger warnings for use during pregnancy.
>
> As set forth above, to prevail, GSK essentially has to show that the CBE process was not available to it or that the FDA would not have approved the proposed label. As to the latter, GSK has to show that the FDA was fully informed as to the relevant science, and that any alleged omission or failure to disclose was not material.

Doc. 1325 at 39–40 (footnote omitted).

The Court then reviewed the evidence submitted by the parties, including the expert report submitted by Plaintiffs from Dr. Brian E. Harvey, a Medical Officer/Supervisory Medical Officer at the FDA between 1995 and 2007, concerning "the completeness of GSK's disclosures and the materiality and likely effect of GSK's alleged omissions. *Id.* at 40. Although GSK contended that it had complied with all regulatory reporting duties and that any undisclosed scientific information was not material, there was no dispute that GSK had failed to disclose full information concerning at least the three Japanese animal studies and certain adverse event data to the FDA. *Id.* at 42 (stating regarding Japanese animal studies: "It is unclear how the Court could conclude on the present record that the 'list' and 'summary' provided to the FDA were complete and accurate."); 45 ("GSK does not seem to contend that it coded adverse event data appropriately in all respects.").[1] In light of Dr. Harvey's testimony that the withheld information was material and would have led the FDA to approve a birth defect warning for Zofran, the Court concluded that there was at least a genuine issue of material fact as to whether the FDA would have approved a warning had it been provided with the withheld information. *Id.* at 44, 46, 48, 49.[2]

[1] GSK did dispute that information concerning the biological mechanism of action, as well as its role in the *Einarson* study, had been withheld from the FDA. Doc. 1325 at 47, 48. As to these matters, this Court concluded that there was at least a "disputed issue of material fact as to whether GSK properly disclosed" the information. *Id.* at 48, 49.

[2] Plaintiffs expect that GSK may renew its objection to this Court's justified consideration of Dr. Brian Harvey's Declaration, as this Court assumed without deciding its admissibility for the purposes of summary judgment. As discussed in Plaintiffs' Response in Opposition to GSK's Motion for Reconsideration at 7, which Plaintiffs incorporate by reference here, the very case on which GSK cites to deny the propriety of relying on Dr. Harvey's Declaration actually stands for the very opposite. *See Cortes-Irizarry v. Corporacion Insular De Seguros*, 111 F.3d 184 (1st Cir. 1997).

Separately, this Court properly concluded that the CBE process was available to GSK to add a birth defect warning to the Zofran label. In particular, the Court rejected GSK's argument that the CBE process was unavailable to alter the "use in specific populations" sections of the labeling. *Id.* at 49–51.

This Court ultimately concluded:

> GSK has not proved, based on the undisputed facts, either (1) that the CBE process was unavailable to it to make more substantial warnings concerning the ingestion of Zofran during pregnancy, or (2) that there is "clear evidence" that the FDA would not have approved a label including such warnings. Accordingly, GSK is not entitled to summary judgment in its favor based on an affirmative defense of federal preemption.

Id. at 51. In so ruling, the Court acknowledged that "the legal framework for considering preemption claims is muddy at best" and that the Court was deciding the issue "without the benefit of . . . guidance" that the Supreme Court might provide when it eventually decided the *Merck* case.

The Supreme Court Ruling in *Merck Sharp & Dohme Corp. v. Albrecht*

On May 20, 2019, the Supreme Court handed down its decision in the *Merck* case, vacating the ruling of the Third Circuit and remanding the case for further proceedings consistent with the guidance provided by the Court in its ruling. In one significant respect, the Supreme Court disagreed with this Court's ruling: it held that the question of "clear evidence" preemption "is a legal one for the judge, not a jury." 2019 WL 2166393, at *9. The Court recognized that "sometimes contested brute facts will prove relevant to a court's legal determination about the meaning and effect of an agency decision," offering as an example a case in which "the FDA rejected a drug manufacturer's supplemental application to change a drug label on the ground that the information supporting the application was insufficient to warrant a labeling change," but the litigants "dispute whether the drug manufacturer submitted all material information to the FDA." *Id.* Even in these circumstances, the Court concluded, the judge, rather than the jury, is the "'better positioned' decisionmaker" to decide the preemption question. *Id.*

The remainder of the Supreme Court's opinion strongly reinforces this Court's conclusion that preemption is inappropriate on the facts before this Court. The Court emphasized that the federal preemption defense must be narrowly cabined to situations in which "the relevant federal and state laws 'irreconcilably conflict[t].'" *Id.* at *8 (quoting *Rice v. Norman Williams Co.*, 458 U.S. 654, 659 (1982)). "'The existence of a hypothetical or potential conflict is insufficient to warrant the pre-emption of the state [law].'" *Id.*; *see also id.* ("'the possibility of impossibility [is] not enough'") (quoting *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 625 n.8). Because "the FDA's CBE regulation . . . permits drug manufacturers to change a label to 'reflect newly acquired information' if the changes 'add or strengthen a . . . warning' for which there is 'evidence of a causal association,' without prior approval from the FDA," "a drug manufacturer will not ordinarily be able to show that there is an actual conflict between state and federal law such that it was impossible to comply with both." *Id.* In such a case,

> showing that federal law prohibited the drug manufacturer from adding a warning that would satisfy state law requires the drug manufacturer to show [both] that it fully informed the FDA of the justifications for the warning required by state law and [also] that the FDA, in turn, informed the drug manufacturer that the FDA would not approve changing the drug's label to include that warning.

Id. at *7.[3]

Justice Thomas's concurring opinion reiterates these conclusions. He writes that "Merck's primary argument . . . is that the FDA would have rejected a hypothetical labeling change submitted via the CBE process. But neither agency musings nor hypothetical future rejections constitute pre-emptive 'Laws' under the Supremacy Clause." *Id.* at *11 (Thomas, J., concurring); *see also id.* at *12 ("hypothetical agency action is not 'Law.' . . . Merck's belief that the FDA would have eventually rejected a CBE application does not make an earlier CBE change

[3] The Supreme Court also declared that "the only agency actions that can determine the answer to the pre-emption question, of course, are agency actions taken pursuant to the FDA's congressionally delegated authority." *Id.* at *8.

impossible.").

Implications of *Merck* Decision for this Court's Summary Judgment Ruling

Nothing in the Supreme Court decision in *Merck* should compel this Court to reopen its consideration of GSK's motion for summary judgment or alter its decision to deny GSK's federal preemption defense. To be sure, the Supreme Court ruling does depart from this Court's February 5 decision in holding that the "clear evidence" preemption question is a question of law to be decided by the court. Nevertheless, because the Supreme Court expressly limits such preemption to cases of actual, irreconcilable conflict between the mandates of state law and formal FDA actions determining a defendant's obligations under federal law, there can be no preemptive conflict here.

As discussed above, there is no dispute in this MDL that the FDA never considered—let alone rejected—a birth defect warning for Zofran with full knowledge of all of the material scientific information that would have supported such a warning. GSK did not dispute that it had failed to disclose full information concerning at least the three Japanese animal studies and certain adverse event data to the FDA. Doc. 1325 at 42, 45.[4] Because the FDA's rejection of the warnings

[4] GSK does contend that it complied with all of its disclosure obligations under federal law, an issue as to which this Court held "it appears at a minimum that there is a disputed issue of material fact." *Id.* at 44 (regarding Japanese animal studies); *see also id.* at 46 (regarding adverse event data). But, as *Merck* makes abundantly clear, the issue whether GSK was obliged by federal regulations to disclose this material scientific information to the FDA is largely irrelevant to the preemption inquiry. The CBE regulation allows a drug manufacturer to add or strengthen a label warning based on "newly acquired information" concerning a drug's risks, 21 C.F.R. § 314.70(c)(6)(iii)(A); there is no requirement that such new information be information that the manufacturer is required to submit to the FDA. Because GSK failed to disclose this information to the agency, the FDA never took any formal agency action to reject a labeling change supported by this information, and thus any purported conflict between the requirements of state and federal law is entirely "hypothetical" and insufficient to support preemption. *Merck*, 2019 WL 2166393, at *8; *see also id.* at *11 (Thomas, J., concurring). This Court reached the same conclusion in its summary judgment ruling. Doc. 1325 at 40 ("to prevail, GSK essentially has to show . . . that the FDA was fully informed as to the relevant science" in rejecting the warning required by state law).

proposed in the citizen petition and in Novartis's supplemental application were based on less than full information, there is no actual, irreconcilable conflict between state and federal law.[5] Any purported conflict between the requirements of state law and FDA labeling determinations based on all of the material scientific information concerning the risks of birth defects associated with Zofran use during pregnancy are only "'hypothetical or potential conflict[s] . . . insufficient to warrant the pre-emption of [state law].'" *Merck*, 2019 WL 2166393, at *8 (quoting *Rice*, 458 U.S. at 659). There is, therefore, no reason for this Court to reopen its consideration of the preemption issue or to depart from its prior conclusion that GSK's summary judgment motion based on federal preemption should be denied.

Respectfully submitted,

/s/ Robert K. Jenner
Robert K. Jenner (BBO No. 569381)
JENNER LAW, P.C.
1829 Reisterstown Road, Suite 350
Baltimore, MD 21208
410-413-2155
rjenner@jennerlawfirm.com

Tobias L. Millrood
POGUST MILLROOD LLC
8 Tower Bridge, Suite 940
Conshohocken, PA 19428
610-941-4204
tmillrood@pbmattorneys.com

[5] The Supreme Court in *Merck* spoke only in the context of a drug manufacturer seeking to avail itself of clear evidence preemption after the manufacturer itself fully informs the FDA of the justifications for a label change—and did not to speak to a drug company seeking preemption by way of a Citizen's Petition or another drug company's request for a label change. Plaintiffs do not concede that GSK is entitled to the benefit of preemption even where it did not request a label change (as it never did), but note that this Court does not need to reach this issue because the FDA lacked material scientific information that had been withheld by GSK when it considered both the citizen petition and Novartis's supplemental application.

Kimberly D. Barone Baden
MOTLEY RICE LLC
28 Bridgeside Boulevard
Mount Pleasant, SC 29464
843-216-9265
kbarone@motleyrice.com

M. Elizabeth Graham
GRANT & EISENHOFER P.A.
123 S. Justison Street
Wilmington, DE 19801
302-622-7099
egraham@gelaw.com

James D. Gotz
HAUSFELD
One Marina Park Drive, Suite 1410
Boston, MA 02210
617-207-0600
jgotz@hausfeld.com

Attorneys for Plaintiffs

Dated: June 3, 2019

CERTIFICATE OF SERVICE

I hereby certify that the foregoing Plaintiffs' Memorandum Related to GSK's Motion For Summary Judgment Based On Federal Preemption in Light of *Merck Sharp & Dohme Corp. v. Albrecht*, which was filed with the Court through the CM/ECF system, will be sent electronically to all registered participants as identified on the Notice of Electronic Filing and paper copies will be sent via first class mail to those identified as non-registered participants.

/s/ *Robert K. Jenner*
Robert K. Jenner